

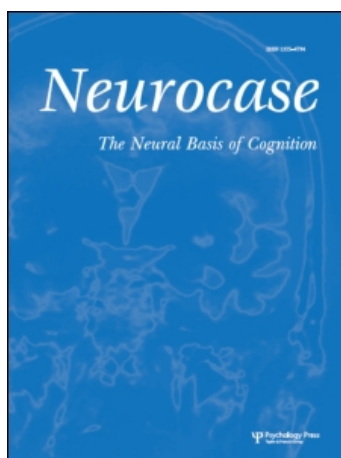
This article was downloaded by: [University of Cambridge]

On: 3 March 2009

Access details: Access Details: [subscription number 908310496]

Publisher Psychology Press

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Neurocase

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title-content=t713658146>

Savant Memory for Digits in a Case of Synaesthesia and Asperger Syndrome is Related to Hyperactivity in the Lateral Prefrontal Cortex

Daniel Bor ^a; Jac Billington ^b; Simon Baron-Cohen ^b

^a Medical Research Council Cognition and Brain Sciences Unit, Cambridge, UK ^b Department of Psychiatry, Autism Research Centre, University of Cambridge, Cambridge, UK

First Published on: 31 March 2008

To cite this Article Bor, Daniel, Billington, Jac and Baron-Cohen, Simon(2008)'Savant Memory for Digits in a Case of Synaesthesia and Asperger Syndrome is Related to Hyperactivity in the Lateral Prefrontal Cortex',*Neurocase*,13:5,311 — 319

To link to this Article: DOI: 10.1080/13554790701844945

URL: <http://dx.doi.org/10.1080/13554790701844945>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Savant Memory for Digits in a Case of Synaesthesia and Asperger Syndrome is Related to Hyperactivity in the Lateral Prefrontal Cortex

DANIEL BOR¹, JAC BILLINGTON² and SIMON BARON-COHEN²

¹Medical Research Council Cognition and Brain Sciences Unit, Cambridge, UK

²Department of Psychiatry, Autism Research Centre, University of Cambridge, Cambridge, UK

Single case: DT is a savant with exceptional abilities in numerical memory and mathematical calculations. DT also has an elaborate form of synaesthesia for visually presented digits. Further more, DT also has Asperger syndrome (AS). We carried out two preliminary investigations to establish whether these conditions may contribute to his savant abilities. *Neuroimaging:* In an fMRI digit span study, DT showed hyperactivity in lateral prefrontal cortex when encoding digits, compared with controls. In addition, while controls showed raised lateral prefrontal activation in response to structured (compared to unstructured) sequences of digits, DT's neural activity did not differ between these two conditions. In addition, controls showed a significant performance advantage for structured, compared with unstructured sequences whereas no such pattern was found for DT. We suggest that this performance pattern reflects that DT focuses less on external mathematical structure, since for him all digit sequences have internal structure linked to his synaesthesia. Finally, DT did not activate extra-striate regions normally associated with synaesthesia, suggesting that he has an unusual and more abstract and conceptual form of synaesthesia. This appears to generate structured, highly-chunked content that enhances encoding of digits and aids both recall and calculation. *Neuropsychology:* People with AS preferentially attend to local features of stimuli. To test this in DT, we administered the Navon task. Relative to controls, DT was faster at finding a target at the local level, and was less distracted by interference from the global level. *Discussion:* The propensity to focus on local detail, in concert with a form of synaesthesia that provides structure to all digits, may account for DT's exceptional numerical memory and calculation ability. This neural and cognitive pattern needs to be tested in a series of similar cases, and with more constrained control groups, to confirm the significance of this association.

Keywords: Prodigy; fMRI; Digit span; Chunking; Asperger syndrome; Synaesthesia.

Introduction

DT is a savant with exceptional abilities in numerical memory and mathematical calculation. For instance, DT successfully memorized Pi to 22,514 decimal places (earning the prize of European Champion), and is able to rapidly complete mental calculations, such as multiplying any two six-digit numbers together. While some memory experts accomplish similar feats after extensive training, this does not explain DT's abilities, since he has had no

explicit training. Rather, his abilities are associated with a complex, multi-modal form of synaesthesia, together with Asperger syndrome (AS) (Baron-Cohen et al. 2007). The nature of his abilities resembles that of Shereshevsky (S), the mnemonist comprehensively studied by Luria (1966), whose synaesthesia included similarly rich percepts, intimately tied to his exceptional memory. (It is unknown if Shereshevsky had AS, as his case predates the recognition of AS.) In order to investigate the differences between DT and the normal population, we carried

We thank DT and the other volunteers for their participation in the study, the radiographers at the Wolfson Brain Imaging Centre for their assistance, Dr Matthew Brett and Dr Rik Henson for technical assistance, and MaryAnn Noonan for help with behavioural analyses. Julian Asher kindly confirmed the diagnosis of DT's synaesthesia using the Test of Genuineness-Revised. We are grateful to Martin Weitz and the production team of 'Brain Man' (Focus Productions) for introducing us to DT as part of their science documentary. This work was supported by the MRC, UK. This study is dedicated to the memory of the late Professor Ati Hermelin, who inspired us to test if DT had AS, given her research into savantism in autism.

Address correspondence to Daniel Bor, Medical Research Council Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge CB2 7EF, UK. E-mail: daniel.bor@mrc-cbu.cam.ac.uk

out a neuroimaging and a neuropsychological experiment, comparing DT with standard control groups.

Synaesthesia is defined as occurring when stimulation of one sensory modality automatically triggers a perception in a second modality, in the absence of any direct stimulation to this second modality (Baron-Cohen, Wyke, & Binnie 1987). The condition is normally evident from an early age, typically before the age of 4 years old. Various forms of synaesthesia have been documented (Baron-Cohen & Harrison 1996), such as coloured taste or coloured touch. Coloured graphemes is the most widely studied type of synaesthesia, and whilst the early estimates of prevalence suggested a rate of at least 1 in 2000 (Baron-Cohen, Burt, Smith-Laittan, Harrison, & Bolton 1996), more recent estimates suggest it may be as common as 1% (Simner et al. 2006). Like most synaesthetes, DT reports having synaesthesia for as long as he can remember, at least from the age of 4 years old, before which we typically have infantile amnesia. For this reason, synaesthesia is distinguished into developmental and acquired forms, the common form being developmental. It is thought to reflect atypical neural connectivity (Grossenbacher & Lovelace 2001; Maurer 1997), which is itself a result of genetic factors (Baron-Cohen, Harrison, Goldstein, & Wyke 1993).

For DT, a visually presented number stream commonly creates a complex 3D mental landscape, varying in size, texture, form and colour. While some synaesthetes demonstrate talent in fields related to their synaesthetic percepts (Smilek, Dixon, Cudahy, & Merikle 2002), such cases are rare. In this paper we report a preliminary study that tests, using fMRI, whether the form of synaesthesia DT has is different from common forms of synaesthesia studied. If so, DT might instead belong to a rare subgroup of synaesthesia, of which S could be another member. Imaging studies of synaesthesia have shown that synaesthetes' extra-modal percepts activate corresponding sensory regions (Nunn et al. 2002; Paulesu et al. 1995). For instance, our earlier study (Nunn et al. 2002) found that those synaesthetes who see colours when hearing spoken words show significantly greater activity in the colour region of the visual cortex, V4, for such auditory stimuli, compared to controls, or when listening to tones alone. If DT was similar to such synaesthetes, his percepts of non-coloured stimuli should activate V4 and other extrastriate regions in an analogous fashion. However, if DT has a markedly different form of synaesthesia, these regions may be silent while other regions may instead be additionally activated. We tested these two possibilities by using visually presented black digits as stimuli in an fMRI experiment.

One factor linked with superior memory recall performance is chunking. Chunking involves reorganizing material into familiar or regular structures and can improve memory performance substantially (Ericsson,

Chase, & Falloon 1980). In many domains, including language acquisition and chess (Bryan & Harter 1899; Chase & Simon 1973; Gobet et al. 2001), chunking is a major factor that increases expertise. For instance, in one study a normal volunteer, using a chunking strategy, increased his digit span performance to 80 digits (Ericsson et al. 1980). Imaging studies examining chunking have associated this process with the lateral prefrontal cortex (LPFC) (Bor & Owen 2007; Bor, Duncan, & Owen 2001; Bor, Duncan, Wiseman, & Owen 2003; Bor, Cumming, Scott, & Owen 2004). For instance, when participants are instructed to memorize novel sequences of either mathematically structured (e.g., 24689753) or random digit sequences, digit span performance was significantly better for the structured sequences and encoding structured digit sequences was associated with increased activity in the LPFC. Since DT's synaesthesia provides perceptual structure to digit sequences, we predicted that, using the same fMRI paradigm, DT would demonstrate increased LPFC activity for all digit sequences, regardless of their level of structure.

In addition to having synaesthesia, DT also has a diagnosis of AS. This diagnosis was made by our team and is reported elsewhere (Baron-Cohen et al. 2007). His AS was consistent with the fact that savant abilities are significantly associated with autism and AS (Hermelin 2002). AS is diagnosed on the basis of difficulties in social and communication development, as well as repetitive and/or unusually narrow ('obsessive') interests (DSM IV; APA 1994). Individuals with AS share these features but, unlike those with autism, do not show language or developmental delay. AS is associated with a particular cognitive style sometimes described as 'weak central coherence' (WCC) (Frith 1989; Happe 1996). According to WCC theory, individuals with autism spectrum conditions (ASC) are more likely to process information in a local, piecemeal fashion, disembedded from the global percept. This results in a reduced propensity to use context. Whilst WCC theory is still a matter of debate (Baron-Cohen & Belmonte 2005), there is a consensus that in ASC attention is preferentially at the local level with evidence of superior attention to detail (O'Riordan, Plaisted, Driver, & Baron-Cohen 2001) and an ability to ignore global level distractors (Ring et al. 1999). Such an attentional style provides some explanation for the obsessional interests and occasional savant-like capabilities seen in individuals with ASC (Hermelin 2002). This narrow focussing of attention may lead to heightened abilities in one particular area (Baron-Cohen, Wheelwright, Stone, & Rutherford 1999; Hermelin 2002).

The relationship between local versus global preference and interference has been widely studied using the Navon task (Navon 1977). A Navon figure consists of hierarchically organised visual stimuli in which a larger (global) letter is composed of smaller (local) letters.

Stimuli can be either congruent (if the local letters are identical to the global letter) or incongruent (if the local and global letters are different). In the incongruent conditions the identification of a target letter at either level gives an indication of the degree of interference from the unattended level as well as the level individuals automatically attend to if not directed.

This can be referred to as either a local or global precedence effect. The former is associated with a preference for local detail (local advantage) and an ability to ignore gestalt distracters (low global interference). The latter is associated with a preference for the global percept (global advantage) and an ability to ignore local level distracters (low local interference). Studies with individuals with ASC have found that, relative to controls, a local precedence is more common (Plaisted, Swettenham, & Rees 1999), reflecting not only a tendency to attend to local level details, but also a relative strength in ignoring global level perceptual distracters (Mottron, Burack, Iarocci, Belleville, & Enns 2003; Plaisted et al. 1999). We used the Navon task on DT and controls in order to test whether DT differentially attends to local details. Such a result might suggest that this particular cognitive style, associated with AS, is related to DT's exceptional abilities.

Methods

Digit span task

Participants

At the time of the research, DT was a right-handed 26-year-old male synaesthete with AS. He has set the European record for memorizing Pi. Despite being diagnosed with AS, DT leads a relatively normal life. He lives with a partner, and is self-employed, primarily offering online language courses. He has a facility for language learning and claims to speak approximately 10 languages. Full details of DT are available elsewhere (Baron-Cohen et al. 2007; Tamm et al. 2006), including his early development and validation of his two diagnoses. In the current study he was compared with 14 right-handed healthy participants who did not have synaesthesia (12 female, aged 19–37). All participants were free from psychiatric or neurological disorders. All participants were scanned for approximately 40 min of echo planar imaging (EPI) and 15 min for a structural scan. All participants gave informed, written consent for participation in the study after its nature and possible consequences had been explained to them. The study was approved by the Local Research Ethics Committee.

Task details

The digits one to nine, spoken by a native English speaking male, were recorded using a Digital Audio Tape

(DAT) recorder at a 44.1-kHz sampling rate and 16 bits per sample. DAT recordings were made in a sound-proof room with recording equipment located outside the room. These were down-sampled to 22.05-kHz mono sound files, for playback using headphones in the scanner.

All sequences were eight digits in length. Two different types of sequence were presented. Structured sequences were made up of portions no longer than five digits in length of runs of either ascending or descending adjacent, even or odd numbers. An example of a structured sequence is 8 6 4 2 3 5 7 9. Unstructured sequences had no two contiguous numbers that followed any type of structured pattern (adjacent, even or odd runs). In addition, the unstructured sequences were designed to appear to be as random as possible, by avoiding any other type of obvious pattern (e.g., involving simple arithmetic patterns such as 3 6 9). Due to these constraints, the numerical distance between any two contiguous digits in a given sequence was generally greater if it was unstructured than if it was structured. An example of an unstructured sequence is 5 1 8 2 7 4 9 6.

For each trial, participants were visually presented with a cross, to indicate the start of the auditory presentation of a novel sequence of eight digits. Each digit was presented for 0.75 s. Following this, there was a variable delay of between 4 and 8 s, after which the word 'RECALL' was visually presented to indicate that the participants were verbally to respond by repeating the sequence exactly as they had just heard it. From the commencement of the response to the start of the subsequent trial there was a variable delay of between 12.5 and 16.5 s. Participants were not informed that there were different types of trials. The different trial types were pseudo-randomly interleaved during each run. Fourteen trials were presented for each run, and two runs were given to each participant, in addition to an initial practice session outside the scanner.

fMRI data acquisition and analyses

Participants were scanned on a 3T Bruker scanner using a head coil. Functional images were collected using 21 slices covering the whole brain (slice thickness 4 mm, inter-slice distance 1 mm, in-plane resolution 3.91×3.91 mm) with an echo planar imaging sequence (TR = 1.1 s, TE = 27.5 ms, flip angle = 65.5 degrees). A total of 540 scans were acquired per run, including 18 dummy scans.

All fMRI data were processed and analyzed using SPM99 software (Wellcome Department of Cognitive Neurology, London). Prior to analysis, all images were corrected for slice timing, with the middle slice in each scan used as a reference. Images were realigned with respect to the first image using trilinear interpolation, creating a mean realigned image. Using the mean realigned image, all images were normalized using affine and smoothly non-linear transformations to an EPI template in Montreal Neurological Institute (MNI) space. Finally,

all normalized images were spatially smoothed with a 10-mm full width half maximum Gaussian kernel.

For the analysis, each trial was split into three events: encoding, delay and retrieval. Single subject statistical contrasts were set up by using the general linear model to fit each voxel with a combination of functions derived by convolving the standard haemodynamic response with the time series of the events and removing low-frequency noise with a high-pass filter. DT was compared with the control group at the random effects level using a one-way ANOVA. All reported peaks were from the random effects analysis, had to pass a whole-brain false detection rate (FDR) (Benjamini & Hochberg 1995; Genovese, Lazar, & Nichols 2002) threshold of $p < .05$, and were required to be at least 20 voxels in volume. The FDR approach controls for the expected proportion of false positives among suprathreshold voxels. An FDR threshold is determined from the observed p -value distribution, and hence is adaptive to the amount of signal within a given contrast (Genovese et al. 2002).

All reported coordinates underwent a transformation from normalized MNI space to Talairach space (www.mrc-cbu.cam.ac.uk/Imaging/mnispaces.html), in order to ascertain more precisely the site of activation relative to the atlas of Talairach and Tournoux (1988).

An additional region of interest (ROI) analysis was carried out to directly test two questions when comparing DT and the control group: (1) whether there was differential activation in extra-striate cortex for encoding digits; and (2) whether there was differential prefrontal activation for the structured, compared with the unstructured digits. A synaesthesia-associated region in V4/8 (spheres of 10-mm radius with centre + or -33 -66 -13), taken from (Nunn et al. 2002) was used to test for extra-striate activation. Due to the extensive multimodal synaesthetic percepts that DT experiences, additional anatomically defined visual region ROIs were used: left and right cuneus, calcarine sulcus, fusiform gyrus and lingual gyrus. For the prefrontal ROIs, *a priori* regions were taken from a previous meta-analysis of prefrontal cortex responses to demanding tasks (Duncan & Owen 2000) and including left and right ventrolateral prefrontal cortex (VLPFC) and dorsolateral prefrontal cortex (DLPFC) regions (left VLPFC: -36 18 1; right VLPFC: 36 18 1; left DLPFC: -42 24 25; right DLPFC: 42 24 25). In order to analyze the ROIs, the MarsBaR software suite was used (<http://marsbar.sourceforge.net/>). This generates t values from mean voxel values for each ROI for a given contrast.

Navon task

Participants

DT (see details above) was tested along with 9 male and 11 female right-handed controls (aged 20–26) drawn

from a student population. All participants were free from psychiatric or neurological disorders. Participants gave informed, written consent for participation in the study after its nature and possible consequences had been explained to them. The study was approved by the Local Research Ethics Committee.

Task details

Letter stimuli (A, H, K and X) were employed for this version of the Navon task (see Figure 1 for dimensions). Each stimulus comprised of a larger letter composed of smaller letters. Participants made a binary button box response to indicate whether or not they detected an A on the screen. Each stimulus was presented for 665 ms, with an inter-stimulus duration of 1150–1300 ms. There were six types of stimuli: congruent (large A made of smaller A's); local (either large X, H or K made of small A's); global (large A made of H's, K's or X's); congruent control stimuli (containing no A's); non-congruent control stimuli (containing no A's) and a '+' fixation condition. There were 12 blocks in which the congruent, local and global stimuli were pseudo-randomly presented a total number of 36 times each. The control (no A) stimuli

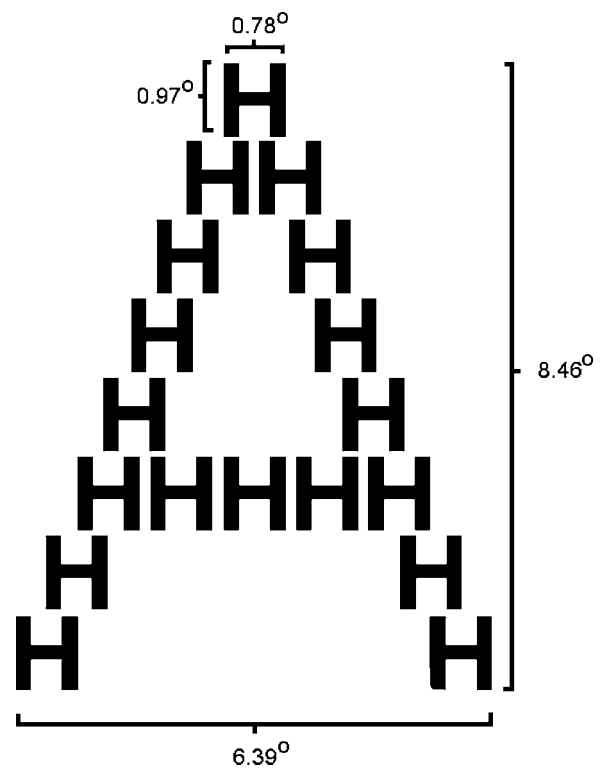


Fig. 1. An example of global condition stimuli in the Navon task. Each stimulus comprised of a larger letter composed of smaller letters. Participants made a binary button box response to indicate whether or not they detected an A on the screen. The angles at which the stimulus subtends the fovea are shown.

consisted of 108 presentations, 36 of which were congruent. There were also 36 '+' presentations. The purpose of the control stimuli was to balance the number of left (A not present) and right (A present) responses.

Prior to analysis the following agglomerated scores were calculated for the Navon task reaction times:

1. Local advantage effect = global target reaction time (RT) – local target RT (+ve scores indicated a local advantage effect, -ve score indicates a global advantage effect)
2. Local interference = global target RT – (congruent RT + congruent control RT) / 2
3. Global interference = local target RT – (congruent RT + congruent control RT) / 2

Results

Digit span task

Performance results

Each trial was marked out of eight. A single response in a trial was marked correct if it matched the number and temporal position during presentation. DT performed both types of trials with a high degree of accuracy, with no significant difference between structured and unstructured trials (97.9 vs. 98.9% for structured and unstructured trials, respectively). Remarkably, when asked after the scanning session, DT reported that he had not noticed any differences between trials, and was completely unaware that some trials were highly structured. In contrast, when asked afterwards, 85% of control participants recognized that some sequences involved structure, and found these trials easier to perform.

While no performance data was present in the fMRI study for the controls, a separate behavioural study was carried out with identical stimuli and parameters (Bor et al. 2004). In that study, the structured trials were performed significantly more accurately than the unstructured trials (87.6 vs. 81.3% for structured and unstructured trials, respectively; $t = 7.66$, $df = 29$, $p < .01$). When compared with the group, DT was not significantly different on overall average span. However, the control group had a significantly greater performance advantage than DT for structured compared with unstructured trials ($t = 8.88$, $df = 29$, $p < .001$).

Given that sex may influence performance on this task, we tested whether there was any difference between the male and female controls. There was no difference on overall span accuracy between males (84.7%) and females (84.1%) ($t = 0.14$, $df = 28$, $p = .89$). There was also no difference on structured trials accuracy alone between the males (88.2%) and females (86.8%) ($t = 0.31$, $df = 28$, $p = .76$). Finally, there was no difference on

structured trials accuracy alone between the males (81.3%) and females (81.4%) ($t = 0.02$, $df = 28$, $p = .98$).

Neurophysiological results

Unlike the control group, who demonstrated consistent activation in LPFC for structured, compared with unstructured, digits during encoding, no significant LPFC activations were observed in DT at the corrected threshold. At the less conservative threshold of $p = .001$ uncorrected, DT still showed no significant frontal lobe activations in the structured compared with the unstructured conditions. This result is consistent with no performance advantage for DT for these sequences for structured compared with unstructured sequences, in addition to DT's report of no recognition of the structure within any sequence. A whole brain analysis was carried out to investigate the interaction of DT versus controls for structured versus unstructured trials. No significant peaks passed the corrected threshold. In order more sensitively to test this, an ROI analysis was carried out on the same interaction. While no significant ROIs were found for additional activation for DT compared with the control group, a trend towards significant increases in the structured minus unstructured comparison in the left ($p = .052$) and right ($p = .087$) VLPFC was found for controls minus DT.

DT alone showed no significant difference in any ROI for the structured minus unstructured comparison, although in the opposite comparison the right VLPFC ROI exhibited a trend towards raised activity for the unstructured condition ($p = .067$). The control group, in contrast, showed significantly raised activity in all ROIs except the right VLPFC (left DLPFC $t = 2.44$, $p = .015$; right DLPFC $t = 3.71$, $p = .001$; left VLPFC $t = 2.02$, $p = .032$).

In order to ascertain what additional regions were activated by DT compared to controls for the general presentation of digits, the group comparison of DT minus controls for the encoding minus delay (collapsed across conditions) contrast was carried out. Using the more conservative FDR threshold, only two peaks in the left LPFC were observed. However, if the threshold is relaxed to uncorrected $p = .001$, there is a clear bilateral LPFC activation (see Table 1 and Figure 2). Given the earlier fMRI study of synaesthesia had found extra-striate activation, using the same contrast we also specifically examined visual regions that corresponded to DT's extra-modal percepts of colour, form, shape, space and texture. Neither the V4 ROI taken from Nunn et al. (2002), nor the anatomically defined visual ROIs showed any significant activation (all $p > .1$).

In order to rule out the possibility that DT's LPFC hyperactivity result was driven instead by increased rehearsal processing by the controls, we examined the

Table 1. Areas of significantly greater activation for DT compared with controls for the contrast: encoding minus delay

Brain regions and Brodmann areas	Coordinates			Cluster volume (voxels)	<i>t</i> -Score
	<i>x</i>	<i>y</i>	<i>Z</i>		
R lateral frontal					
47	48	29	-12	7	6.13
45	53	27	7		5.4
45	56	21	13		5.34
44	56	16	21	18	5.64
4	59	-4	28	1	3.9
4/43	62	-8	20	4	6.02
Medial frontal					
10/32	-12	34	-9	20	8.89
L lateral frontal					
47	-50	32	-2		7.58
47	-39	31	-17	31	8.63
44/9	-56	13	19	73	13.45*
44	-59	7	13		6.89*
Subcortical					
Cerebellum	-9	-76	-14	11	5.39

All reported peaks passed an uncorrected threshold of $p = .001$. All peaks with an asterisk passed the more conservative whole-brain false detection rate (FDR) (Benjamini & Hochberg 1995; Genovese et al. 2002) threshold of $p < .05$, and were required to be at least 20 voxels in volume. Coordinates underwent a transformation from normalized MNI space to Talairach (Talairach & Tournoux 1988). Activation peaks without volume details belong to the cluster of the last reported volume.

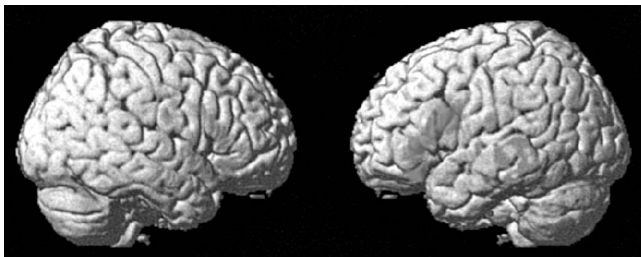


Fig. 2. Regions of increased activation for DT versus control group for contrast of encoding minus delay (collapsed across trial type). For illustration purposes, activations shown pass an uncorrected whole brain threshold of $p = .001$, rendered onto the canonical T1-weighted brain image of SPM 99. To view this figure in color, please visit the online version of this issue.

ROI differences in activation during encoding for DT and controls (see Figure 3). DT generally showed greater increases in activity compared to baseline than controls, although this pattern was less marked for the structured than unstructured condition. To confirm that these differences were significant, we carried out an ROI analysis comparing DT with controls during the encoding of

structured and unstructured trials separately. For the unstructured encoding events DT showed significant increases in activation in all the ROIs (left DLPFC $t = 2.92$, $p = .006$; right DLPFC $t = 2.16$, $p = .025$; left VLPFC $t = 4.17$, $p < .001$; right VLPFC $t = 5.15$, $p < .001$). For the equivalent structured comparison, all ROIs except the right DLPFC were significantly increased for DT, albeit numerically less strongly than for the unstructured comparison (left DLPFC $t = 2.52$, $p = .013$; left VLPFC $t = 3.05$, $p = .005$; right VLPFC $t = 4.03$, $p < .001$).

Given that the majority of controls were of a different sex to DT, we tested whether there were any differences in activation between males and females. Examining the main control contrast of structured minus unstructured trials during encoding, no differences between male and female activations were found in either the peak whole brain activation ($-56\ 21\ 4$) (Mann-Whitney $Z = 1.47$, $p = .14$), or the two significant ROIs (left VLPFC: Mann-Whitney $Z = 0.64$, $p = .52$; left DLPFC: Mann-Whitney $Z = 0.18$, $p = .85$).

Navon task

DT had a significantly larger overall local advantage effect relative to controls who exhibited neither a local nor a global advantage effect (DT = 58.14, control mean = -2.97 , $SD = 30.71$) ($t = 9.12$, $df = 20$, $p < .001$). Both DT and controls experienced interference from the global level distractor. However, DT experienced significantly less global interference than controls (DT = 25.49, control mean = 57.8, $SD = 33.87$) ($t = 4.37$, $df = 20$, $p < .05$). Similarly, both DT and controls experienced a degree of local interference; however DT experienced significantly more local interference than controls (DT = 80.63, control mean = 54.83, $SD = 37.5$) ($t = 3.15$, $df = 20$, $p < .005$).

Discussion

In this study we tested DT, a single case of numerical memory savantism, who has both synaesthesia and AS. We carried out preliminary behavioural and fMRI tests to compare DT's performance on digit span variants and the Navon task, a test of local or global attentional bias, with normal controls. The fMRI digit span task demonstrated that DT processes number sequences differently to controls. Thus, when presented with numerical stimuli that for him generated multimodal and highly structured synaesthetic percepts, DT showed hyperactivity in bilateral LPFC compared to normal controls. Our previous studies have found that such an activation pattern can be associated with general chunking processes (Bor & Owen 2007;

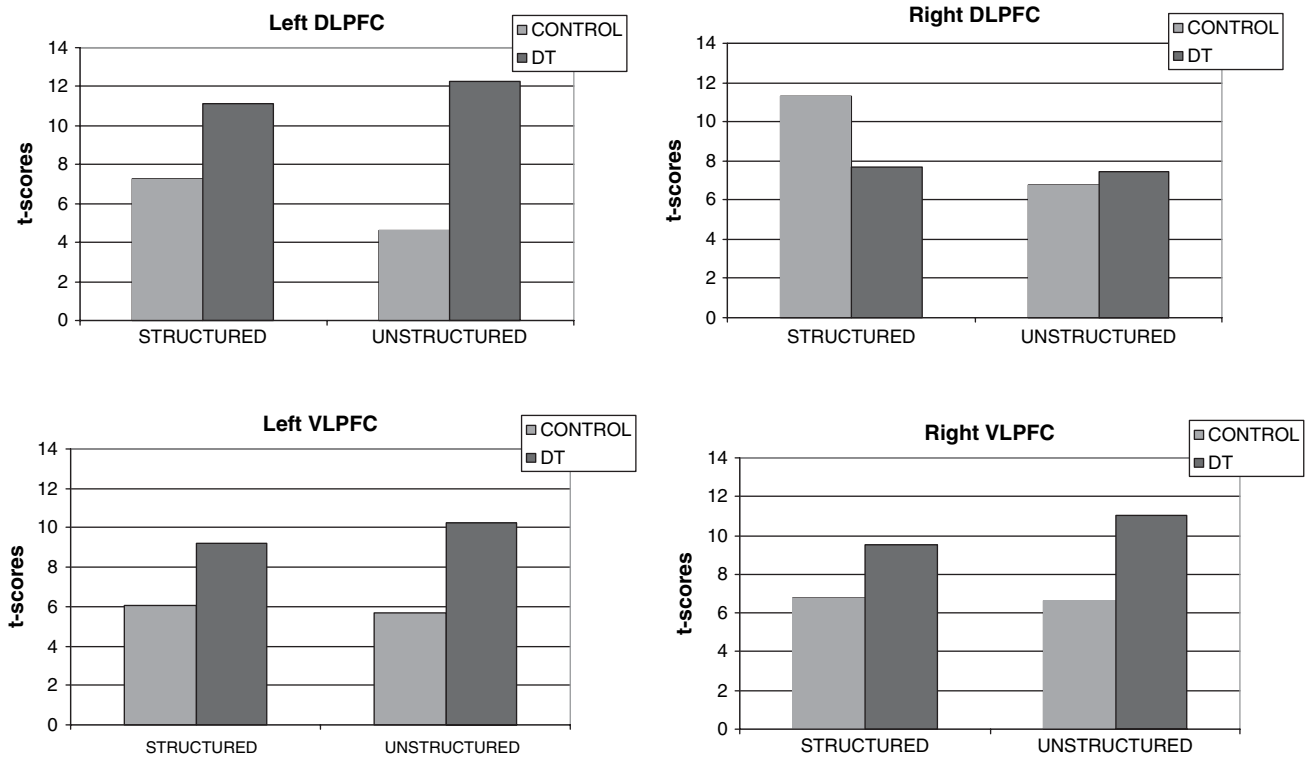


Fig. 3. *t*-Scores for raised activation compared to baseline on four *a priori* regions of interest for DT and the control group during the encoding phase.

Bor et al. 2001, 2003, 2004). Given that DT's synaesthetic representation of all numbers is highly structured and interlinked, it is possible that the over-activity in LPFC in DT reflects chunking processes. An alternative explanation is that DT was using additional working memory processes, which is also associated with LPFC (Cabeza & Nyberg 2000; Wager & Smith 2003). This seems unlikely, however, given that there was no performance difference between DT and controls, and that his digits WM capacity was greater than controls (Baron-Cohen et al. 2007).

Previous studies of synaesthesia have reported additional sensory activation when compared to normal controls, corresponding to the extra-modal percepts in synaesthesia (Nunn et al. 2002). However, we did not find any such activation pattern in DT when compared to normal controls. This, in combination with DT's LPFC hyperactivity, and his description of the unusually multifaceted nature of his perceptual representation for digits, suggests DT may have a different form of synaesthesia than the perceptual form that is more commonly studied. Recent studies have indicated that a subset of synaesthetes have a more conceptual form of the condition, which appears less reliant on visual brain regions (Hubbard, Arman, Ramachandran, & Boynton 2005; Simner & Ward 2006). Although it has yet to be shown which

regions are differentially recruited for this synaesthesia group, a plausible region is the LPFC. We propose that DT lies at the conceptual end of this perceptual-conceptual synaesthesia continuum, and that the abstract, conceptual richness of his experiences gives rise to his exceptional abilities. Further studies comparing DT directly with common perceptual and conceptual synaesthesia groups are clearly needed to test these hypotheses.

While DT may have activated additional LPFC regions because of chunking all digits, he showed no additional propensity to chunk the structured version of the digit span task or show any awareness of such structure, unlike controls who showed a significant advantage for the structured digit span trials, along with a trend towards additional LPFC activity compared to DT. In addition, DT did not activate LPFC more for structured compared with unstructured trials, despite this being a robust finding in the controls. Presumably DT views and chunks numbers primarily via what he describes as his complex 3D 'mental landscape', so that intrinsic mathematical structure is of secondary importance. The fact that DT showed substantially raised VLPFC and DLPFC activity for both structured and unstructured digits supports this interpretation.

Evidence to support the idea that DT (like other cases of AS) has an extreme focus on detail comes from the Navon task, where DT had a propensity to attend to the

local level of the stimuli and experience less global interference than controls. This is consistent with his diagnosis of AS, a condition associated with a locally orientated cognitive style. Note that excellent attention to detail is predicted both by (WCC) (Frith 1989; Happe 1996) and the hyper-systemizing models (Baron-Cohen 2006). Where these two models diverge is that the WCC model predicts difficulties with integration, and therefore poor understanding of a whole system, whilst the hyper-systemizing model predicts that using the local detail strategy and working outwards, people with AS could achieve excellent understanding of a whole system, especially if the system is highly predictable or structured. Good understanding of physical-mechanical systems has been found in AS (Baron-Cohen et al. 2001; Lawson, Baron-Cohen, & Wheelwright 2004), suggesting integration is not globally impaired in ASC and supporting preserved or even superior systemizing. In concordance with this, DT reported unusual structured associations with any number we presented to him, seeing even very large numbers as the products of two smaller ones.

While local processing can occasionally cause disruption to performance, it may also help to reduce the amount of interference from conflicting distracters or contextual preconceptions. Local processing can also facilitate binding together contiguous stimuli in a sequence, and aid the chunking of such stimuli. It helps explain why DT might focus more closely on a specific, logical domain, such as numbers, relative to controls.

While other neurophysiological studies have investigated those from the normal population with superior memories resulting from extensive practice (Maguire, Valentine, Wilding, & Kapur 2003), there are few studies that have examined both the neural and psychological mechanisms of a validated savant. Our preliminary experiments suggest that DT's exceptional numerical abilities relate to hyperactivity in the LPFC and stem from a combination of his distinct form of synaesthesia and the cognitive style that arises from AS. An important next step will be to examine other savants like DT, to ascertain the relative contribution of synaesthesia and AS to their abilities, and whether they have a similar pattern of neural activation. In addition, further studies are needed directly to compare DT on current and related tasks with synaesthesia and AS groups. It will be challenging to find an appropriate synaesthesia control group, given the unusual nature of DT's synaesthesia. However, this comparison will be crucial to validate the claim that it is the combination of multimodal synaesthesia and AS that provides DT with the exceptional abilities that he possesses.

References

- APA (1994). *DSM-IV diagnostic and statistical manual of mental disorders*. Arlington, VA: American Psychiatric Publishing Inc.
- Baron-Cohen, S. (2006). The hyper-systemizing, assortative mating theory of autism. *Progress in Neuropsychopharmacological and Biological Psychiatry*, 30(5), 865–872.
- Baron-Cohen, S., & Belmonte, M. K. (2005). Autism: A window onto the development of the social and the analytic brain. *Annual Reviews of Neuroscience*, 28, 109–126.
- Baron-Cohen, S., & Harrison, J. E. (1996). *Synaesthesia: Classic and contemporary readings*. Oxford: Blackwell.
- Baron-Cohen, S., Wyke, M. A., & Binnie, C. (1987). Hearing words and seeing colours: An experimental investigation of a case of synaesthesia. *Perception*, 16(6), 761–767.
- Baron-Cohen, S., Harrison, J., Goldstein, L. H., & Wyke, M. (1993). Coloured speech perception: Is synaesthesia what happens when modularity breaks down? *Perception*, 22(4), 419–426.
- Baron-Cohen, S., Burt, L., Smith-Laittan, F., Harrison, J., & Bolton, P. (1996). Synaesthesia: Prevalence and familiarity. *Perception*, 25(9), 1073–1079.
- Baron-Cohen, S., Wheelwright, S., Stone, V., & Rutherford, M. (1999). A mathematician, a physicist and a computer scientist with Asperger syndrome: Performance on folk psychology and folk physics tests. *Neurocase*, 5(6), 475–483.
- Baron-Cohen, S., Wheelwright, S., Spong, A., Schill, V., & Lawson, J. (2001). Are intuitive physics and intuitive psychology independent? A test with children with Asperger Syndrome. *Journal of Developmental and Learning Disorders*, 5, 47–78.
- Baron-Cohen, S., Bor, D., Billington, J., Asher, J., Wheelwright, S., & Ashwin, C. (2007). Savant memory in a man with synaesthesia and Asperger Syndrome. *Journal of Consciousness Studies*, 14 (9–10), 237–251.
- Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society B* 57(1), 289–300.
- Bor, D., & Owen, A. M. (2007). A common prefrontal-parietal network for mnemonic and mathematical recoding strategies within working memory. *Cerebral Cortex*, 17, 778–786.
- Bor, D., Duncan, J., & Owen, A. M. (2001). The role of spatial configuration in tests of working memory explored with functional neuroimaging. *Scandinavian Journal of Psychology*, 42(3), 217–224.
- Bor, D., Duncan, J., Wiseman, R. J., & Owen, A. M. (2003). Encoding strategies dissociate prefrontal activity from working memory demand. *Neuron*, 37(2), 361–367.
- Bor, D., Cumming, N., Scott, C. E., & Owen, A. M. (2004). Prefrontal cortical involvement in verbal encoding strategies. *European Journal of Neuroscience*, 19(12), 3365–3370.
- Bryan, W. L., & Harter, N. (1899). Studies on the telegraphic language: The acquisition of a hierarchy of habits. *Psychological Review*, 6, 345–375.
- Cabeza, R., & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience*, 12(1), 1–47.
- Chase, W. G. and Simon, H. A. (1973). 'Perception in Chess.' *Cognitive Psychology*, 4, 55–81.
- Duncan, J., & Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neuroscience*, 23(10), 475–483.
- Ericsson, K. A., Chase, W. G., & Falloon, S. (1980). Acquisition of a memory skill. *Science*, 208, 1181–1182.
- Frith, U. (1989). *Autism: Explaining the enigma*. Oxford: Basil Blackwell.
- Genovese, C. R., Lazar, N. A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage*, 15(4), 870–878.

- Gobet, F., Lane, P. C. R., Croker, S., Cheng, P. C. H., Jones, G., Oliver, L., & Pine, J. M. (2001). Chunking mechanisms in human learning. *Trends in Cognitive Sciences*, 5(6), 236–243.
- Grossenbacher, P. G., & Lovelace, C. T. (2001). Mechanisms of synesthesia: Cognitive and physiological constraints. *Trends in Cognitive Sciences*, 5(1), 36–41.
- Happe, F. G. (1996). Studying weak central coherence at low levels: Children with autism do not succumb to visual illusions. A research note. *Journal of Child Psychology Psychiatry*, 37(7), 873–877.
- Hermelin, B. (2002). *Bright splinters of the mind: A personal story of research with autistic savants*. London: Jessica Kingsley.
- Hubbard, E. M., Arman, A. C., Ramachandran, V. S., & Boynton, G. M. (2005). Individual differences among grapheme-color synesthetes: Brain-behavior correlations. *Neuron*, 45(6), 975–985.
- Lawson, J., Baron-Cohen, S., & Wheelwright, S. (2004). Empathising and systemising in adults with and without Asperger Syndrome. *Journal of Autism and Developmental Disorders*, 34(3), 301–310.
- Luria, A. R. (1966). *The mind of a mnemonist*. Cambridge, MA: Harvard University Press.
- Maguire, E. A., Valentine, E. R., Wilding, J. M., & Kapur, N. (2003). Routes to remembering: The brains behind superior memory. *Nature Neuroscience*, 6(1), 90–95.
- Maurer, D. (1997). Neonatal synaesthesia: Implications for the processing of speech and faces. In S. Baron-Cohen and J. Harrison (Eds), *Synaesthesia: Classic and contemporary readings* (pp. 224–242). Cambridge, MA: Blackwell Publishers.
- Mottron, L., Burack, J. A., Iarocci, G., Belleville, S., & Enns, J. T. (2003). Locally oriented perception with intact global processing among adolescents with high-functioning autism: Evidence from multiple paradigms. *Journal of Child Psychology and Psychiatry*, 44(6), 904–913.
- Navon, D. (1977). Forest before trees: The precedence of global features in visual perception. *Cognitive Psychology*, 9, 353–383.
- Nunn, J. A., Gregory, L. J., Brammer, M., Williams, S. C., Parslow, D. M., Morgan, M. J., Morris, R. G., Bullmore, E. T., Baron-Cohen, S., & Gray, J. A. (2002). Functional magnetic resonance imaging of synesthesia: Activation of V4/V8 by spoken words. *Nature Neuroscience*, 5(4), 371–375.
- O’Riordan, M. A., Plaisted, K. C., Driver, J., & Baron-Cohen, S. (2001). Superior visual search in autism. *Journal of Experimental Psychology: Human Perception and Performance*, 27(3), 719–730.
- Paulesu, E., Harrison, J., Baron-Cohen, S., Watson, J. D., Goldstein, L., Heather, J., Frackowiak, R. S., & Frith, C. D. (1995). The physiology of coloured hearing. A PET activation study of colour-word synaesthesia. *Brain*, 118(Pt 3), 661–676.
- Plaisted, K., Swettenham, J., & Rees, L. (1999). Children with autism show local precedence in a divided attention task and global precedence in a selective attention task. *Journal of Child Psychology and Psychiatry*, 40(5), 733–742.
- Ring, H. A., Baron-Cohen, S., Wheelwright, S., Williams, S. C., Brammer, M., Andrew, C., & Bullmore, E. T. (1999). Cerebral correlates of preserved cognitive skills in autism: A functional MRI study of embedded figures task performance. *Brain*, 122(Pt 7), 1305–1315.
- Simner, J., & Ward, J. (2006). Synaesthesia: The taste of words on the tip of the tongue. *Nature*, 444(7118), 438.
- Simner, J., Mulvenna, C., Sagiv, N., Tsakanikos, E., Witherby, S. A., Fraser, C., Scott, K., & Ward, J. (2006). Synaesthesia: The prevalence of atypical cross-modal experiences. *Perception*, 35(8), 1024–1033.
- Smilek, D., Dixon, M. J., Cudahy, C., & Merikle, P. M. (2002). Synesthetic color experiences influence memory. *Psychology Science*, 13(6), 548–552.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain: 3-Dimensional proportional system: an approach to cerebral imaging*. Stuttgart: Thieme.
- Tammet, D. (2006). *Born on a blue day: A memoir of Aspergers and an extraordinary mind*. London: Hodder & Stoughton Ltd.
- Wager, T. D., & Smith, E. E. (2003). Neuroimaging studies of working memory: A meta-analysis. *Cognitive Affect Behavioural Neuroscience*, 3(4), 255–274.